

New Insulins and Quality of Life

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Abstract. Extreme customization of treatment is even more necessary when dealing with young diabetic patients as compared with adult patients. From diagnosis the pediatrician must introduce treatment in the less traumatic way possible so that the child does not perceive a derangement of his/her life. In order to preserve the quality of life the diabetic child must be able to attend birthday parties, participate in sports, and generally lead a full social life just like his/her friends. In the present paper we evaluate the characteristics of the new insulin analogues and their advantages and disadvantages with respect to the needs of patients. The wide spectrum of available insulin formulations including also the new short- and long- acting insulin analogues are of great help in conceiving a therapeutic plan closely adherent to the patient's needs. As an example, in children aged less than 5-6 years a short acting insulin may be injected immediately after the meal. The same insulin may be useful in older patients with an incostant style of life due to social activities. On the other hand the "old" insulins may still be used for the therapeutic plan in patients with a more constant life style as to the physical exercise and intervals between the meals. In conclusion, the quality of life in the children and adolescents with diabetes may be accomplished with a flexible and personalized therapeutic plan and a great attention to the education. The latter is a very important tool for the compliance and the reduction of anxiety in patients and their parents.

Key words: Insulin analogues, quality of life

Insulin therapy is the factor that most affects the diabetic patient's quality of life because it is unavoidable, strictly connected with the timing of meals and impacts also on the patient's lifestyle. For this reason, insulin therapy may be likened to an artist's palette where the insulins represent the colors and the final painting, quality of life.

The concept of quality of life is very personal; it means different things to different people, even people of the same age. Consequently, insulin schemes should be highly personalized. This is particularly important in the case of children; the diabetologist should try not to derange the child's lifestyle and habits; ideally, the diabetic child should not feel different from his/her friends. Fortunately, the advent of the new insulins has represented a tremendous step

forward in this sense, because, given their different pharmacokinetic profiles, it has become much easier to customize therapy.

We have evaluated the characteristics of insulin analogues and compared their advantages and disadvantages with respect to the needs of patients.

Short-acting insulin analogues

The advantages of short-acting insulin analogues (Lys-ProTM and AspartTM insulin) are: 1) a more flexible lifestyle, because patients can inject insulin immediately before or after a meal (1), and can better adapt the dose to carbohydrate intake; 2) improved 1- and 2-hour post-prandial blood glucose levels compared

with regular human insulin because they peak earlier (2); 3) a decreased risk of nocturnal hypoglycaemia; 4) no need for a mid-morning/afternoon snack (3); and 5) the possibility of administering with easy-to-apply continuous subcutaneous infusion systems (CSII). However, these insulins are not without disadvantages. For instance, their action is short lasting, and NPH must be added to lispro or aspart at mealtimes to maintain blood glucose control late after meals. In addition, patients are forbidden between-meal snacks, the risk of precocious hypoglycaemia increases after the intake of short-acting analogues (4), and multiple glycaemic controls must be made before all injections. Lastly, due to their short half-life, we have experienced more frequent episodes of ketoacidosis during intercurrent illnesses with these new insulins.

These factors probably explain the finding reported by the Italian Study Group on Diabetes of the Pediatric Endocrinology and Diabetology Society that only 35% of Italian pediatric diabetologists use insulin schemes with short-acting analogues and 65% still use 'traditional' regular human insulin (5).

Long-acting insulin analogues

There are two procedures for prolonging insulin action. One is an insulin preparation (Glargine - Lantus™) soluble in acid solution, which precipitates as micro-crystals after injection in the subcutaneous tissue, where the pH is neutral. The other is variant of this molecule that promotes the binding to a serum carrier that has a prolonged half-life, e.g. albumin (Detemir™).

The major advantage of long-acting insulin analogues is delayed and prolonged absorption from the subcutaneous injection site with a relatively constant basal insulin supply consistent with that secreted by non-diabetic subjects (6).

Long-acting insulin analogues are associated with a decreased risk of hypoglycaemia (7), a greater lifestyle flexibility (8), administration by pen and a reduction of the "down phenomenon" (9).

In general, long-acting insulin once daily is combined with short-acting insulin at mealtimes.

Glargine™ insulin has the disadvantage that, be-

cause it is formulated as a clear, acidic solution, it cannot be mixed with short-acting insulin that is formulated at neutral pH. In addition, its effect lasts less than 24 hours, and pre-dinner hyperglycaemia is frequent so that the "down phenomenon" is replaced by an annoying "setting effect". It has been suggested that Glargine™ be administered twice daily (every 12 hours) associated with short-acting insulin at mealtimes (up to five insulin injections/day!). Differently, we have found that by substituting short-acting analogues with regular insulin at lunch the effect of insulin lasts into the afternoon.

Detemir™ is an insulin analogue that has high affinity for albumin. The subcutaneous albumin binding, and consequently increased plasma half-life prolongs the action profile. The advantage of this formulation is that it can be mixed with all other insulins and, probably, the effect lasts longer as compared with Glargine™.

Customizing treatment

Extreme customization of treatment is even more necessary when dealing with young diabetic patients as compared with adult patients. From diagnosis, the child must be "taught" to accept treatment that will be life-long; the pediatrician and the family must introduce treatment in the least traumatic way possible so that the child does not perceive a derangement of his/her life. The diabetic child must be able to attend birthday parties, participate in sports, and generally lead a full social life just like his/her friends. Therefore, therapy must be adapted to the child, not the child to therapy.

However, this concept could be taken to its extreme. For example, beware of homemade preparations comprised predominantly of rapid-acting molecules associated to a lesser proportion of intermediate-acting molecules in order to let the patient to use the pen for administration. Similarly, there are even schemes that foresee only two administrations of rapid+slow insulin (morning and evening) to allow the child to attend school outings without having to use insulin at lunch.

The quality of life is a very vague concept, and

each patient's concept of his/her quality of life is almost unique, and in some, fortunately rare cases, quality of life does not always coincide with therapeutic needs and, with the ultimate aim of preventing microvascular complications. Although the diabetologist must try to meet the patient's needs, this is not always possible even given the wide range of molecules available, because on occasions the patient's desires can go beyond the limits imposed by the disease. This situation brings to mind the Mexican who threw himself, completely nude, on a cactus; when asked why, he replied "I thought it was a good idea!".

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